Background: Tacrolimus (TAC) effectively and selectively suppresses T lymphocyte activity, and is used for GVHD prophylaxis. According to some reports, pre-engraftment immune reactions (PIR) occur early after CBT. During PIR phase, we often experience instability of blood concentration of TAC, and need the dose of the drug adjusted accordingly. There are no reports assessing changes in TAC concentration during the PIR phase.

Patients and Methods: Between July 2003 and November 2013, 105 patients received single-unit cord blood transplantation (CBT) at our institution. We analyzed data for 63 patients for whom only TAC was used for GVHD prophylaxis. The conditioning regimen was myeloablative conditioning regimen for 11 patients and reduced intensity conditioning for 52 patients. We assumed that the blood concentration of TAC would reach a steady state between days 5 to 7 and would be proportional to the dose used. Thus, the average concentration of days 5 to 7 was used as the reference value. TAC dose was adjusted based on blood concentration and patient body weight, and compared with the reference dose until day 40. PIR was diagnosed based on the criteria set forth by Wake et al.

Results: Engraftment was achieved in 59 patients (median, day 25), and 46 developed PIR. The blood concentration of TAC significantly decreased in the PIR group on day 8 ($P < 0.001$), but not in non-PIR group. On days 8, 9, and 10, the adjusted dose of TAC significantly increased in the PIR group ($P < 0.001$, 0.001, and 0.003, respectively) corresponding to the decreased blood concentration of TAC, but not in the non-PIR group.

Conclusions: Decreased blood concentration of TAC and increased requirement of TAC dose in the PIR phase were observed. During the PIR phase, frequent check of the TAC blood concentration and adjustment of the drug should be performed. These phenomena are possibly associated with T lymphocyte activation.

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Economic Consequences of Cytomegalovirus Disease Among Stem Cell Transplant Recipients

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Background: Cytomegalovirus (CMV), a common opportunistic infection among stem cell transplant recipients, is associated with substantial morbidity and mortality. Limited information is available regarding the economic consequences of CMV disease among these patients. The current study evaluated the incremental healthcare costs associated with CMV disease among stem cell transplant recipients.

Methods: Adults with stem cell transplant were identified in the Truven Health MarketScan® database (Q1 2002-Q4 2011). Patients were required to have ≥ 2 years of continuous enrollment following the transplantation. They were classified into the CMV cohort if they had ≥ 1 observed CMV diagnosis within the 2-year period after transplantation (study period), or the No CMV cohort if they did not have any CMV diagnosis during the entire observation period in the database. Patients in the CMV cohort were matched 1:1 to patients in the No CMV cohort in two steps. The first step was exact matching based on age strata, gender, relevant comorbidities, year of transplantation, type of stem cell transplant, and donor type. The second step was a propensity score match based on region of residence, health plan type, relevant comorbidities, and baseline healthcare resource utilization and costs. The costs in the study period were compared between the two matched cohorts using Wilcoxon signed-rank tests.

Table
Healthcare Costs during the 2-Year Study Period: CMV and No CMV Cohorts

Costs categories (2013 USD)	CMV cohort (N =113)	No CMV cohort (N = 113)	Cost difference	P-value
Total costs	586,416.0	305,462.1	280,953.9	<.0001
Medical costs	543,813.1	276,593.3	267,219.7	<.0001
Inpatient services costs	343,691.6	157,995.6	185,696.0	<.0001
Emergency room services costs	4,555.3	5,404.2	-848.9	0.2860
Outpatient services costs	195,566.2	113,193.6	82,372.6	<.0001
Drug costs	42,602.9	28,868.7	13,734.2	0.0079
Subcategories of total costs				
Antiviral drug costs	6,920.6	449.7	6,470.9	<.0001
CMV laboratory test costs	3,357.1	1,473.3	1,883.7	0.0002

Results: Among 189 stem cell transplant recipients with CMV and 2,539 recipients without CMV, a total of 113 matched pairs were identified. The baseline characteristics were comparable between the matched CMV and No CMV cohorts. During the 2-year study period, the CMV cohort was associated with significantly higher costs across all cost categories. The total costs were $586,416 in the CMV cohort vs. $305,462 in the No CMV cohort (incremental cost of $280,954, $p < 0.0001$). The majority of the differences were attributable to the incremental medical costs, accounting for ~95% of the total incremental costs (Table).

Conclusions: Stem cell transplant recipients with CMV disease incurred significantly higher healthcare costs, including costs for CMV lab tests and antiviral drugs, than those without CMV disease.

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Risk Factors for Progression of CMV Viremia to CMV Disease after Allogeneic Hematopoietic Stem Cell Transplantation

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Introduction: Cytomegalovirus (CMV) causes significant morbidity and mortality after allogeneic hematopoietic stem cell transplant (allo-HSCT). Factors associated with progression from CMV viremia to disease despite pre-emptive CMV treatment are poorly defined. We sought to identify risk factors among adult allo-HSCT recipients.

Methods: Retrospective single-center case-control study. The McGill University Health Centre SCT Program database was used to identify adults receiving a first allo-HSCT between January 1, 2006 and February 12, 2013, and who experienced ≥1 episode of CMV viremia detected by polymerase chain reaction (PCR). Medical records of cases (CMV disease) and controls (without disease) were reviewed for the following data: characteristics of recipient, donor, stem cell graft, transplant procedure, viremic episodes, steroid use post-transplant, and occurrence of acute and/or chronic GVHD post-transplant. For analysis, Fisher's exact test or Wilcoxon Rank Sum test (for categorical and continuous variables, respectively) was used. Variables were selected for